REMARKS

Claims 5 and 39-58 were pending. Claim 52 has been cancelled without prejudice. Claims 5, 39-42, 47, 50-51 and 53-56 have been amended. Claims 5, 39-42, 46, 50-51 and 53-56 have been amended to recite the *Xanthomonas campestris* strain (XWCM1/pBBR5BC), support for which may be found in the originally filed specification *inter alia*, at page 10, Table 2 and page 11, [38]. Further support for the amendment of claim 5 to add the method step may be found in the specification as originally filed, *inter alia*, at page 3, [12]. Support for the amendment of claim 39 may be found in the specification as originally filed, *inter alia*, at page 3, [12]. Support for the amendment of claims 40-42 and 47 to insert "the amount of gene product of *gumB* and *gumC*" may be found in the specification as originally filed, *inter alia*, at page 3, [12] and antecedent basis is provided in original claim 39. Support for the amendment of claims 41-42 to insert "selectively increasing the amount of gene product of gumD, *gumE, gumF and gumG*" may be found in the specification as originally filed, *inter alia*, at page 3, [12]-[13] and Figure 1, which shows *inter alia gumD, gumE, gumF* and *gumG*. Support for the amendment of claim 42 to insert "selectively increasing the amount of gene product of" *orfX* may be found in the specification as originally filed, *inter alia*, at page 3, [12]-[13]. Claim 50 provides antecedent basis for the insertion of "*Xanthomonas campestris*" into claims 50-51 and 53-56; support for the recitation of "*gumD, gumE, gumF and gumG*" in claims 50, 53 and 56 may be found in the specification as originally filed, *inter alia*, at Figure 1, which shows *inter alia gumD, gumE, gumF* and *gumG*. Independent claims 5, 39 and 50 have been amended to insert the recitation of ", said gene product of *gumB*, and said gene product of *gumC*," support for which may be found in the specification as originally filed, *inter alia*, at page 9, [32], which provides respective SEQ ID numbers corresponding to the gene products of *gumB* and *gumC, i.e.,* the amino acid sequences encoded by each of these two genes, respectively. No new matter has been added by this amendment. Applicants respectfully request entry of this Amendment. Prompt consideration and action is respectfully requested. The Commissioner is hereby authorized to charge payment of the three-month extension fee, and any other fees required for entry and consideration of this communication, to maintain this application as pending, or credit any overpayment to the deposit account of Hunton & Williams, **Deposit Account Number 50-**

0206. The Examiner is invited to contact the undersigned at the telephone number below if progress of the application could be advanced.

Claim Objections

Claims 52 and 53 have been objected to because should claim 52 be found allowable, claim 53 will be objected to under 37 C.F.R. 1.75 as being a substantial duplicate thereof.

Applicants have cancelled claim 52 without prejudice to obviate this objection. Accordingly, withdrawal of the objection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 50 and dependent claims 52-58 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for recitation in Claims 50, 52 (cancelled hereinabove), 53 and 55 of the phrase "gumD-gumG."

Applicants have amended Claims 50, 53 and 55 to recite "*gumD, gumE, gumF* and *gumG.*" Accordingly, withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Enablement

Claims 5 and 39-58 have been rejected under 35 U.S.C. 112, first paragraph for lack of enablement for encompassing any variant or mutant gene product of *gumB* and *gumC* because the specification allegedly "is enabling for a method of producing a xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by a wild-type strain, wherein said method comprises selectively increasing the amount of wild-type gene product of *gumB* and *gumC* (gumB:XCC2454; gumC:XCC2453, page 8 of specification) by a plasmid comprising said genes, but not genes encoding *orfXor gumD, E, F* and G, in a mutant *Xanthomonas campestris* 2895 culture lacking wild-type *gum* genes (page 7 of specification) and precipitating said high viscosity xanthan preparation. However, it is asserted, the specification does not reasonably provide enablement for a method of producing xanthan composition comprising a population of

xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding orfXor *gumD, E, F* and G in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation."

Applicants have amended independent claims 5, 39 and 50 to recite the selective increase in the specified gene product of *gumB* and *gumC*. Dependent claims 40-49, 51 and 53-58 maintain these recitations by virtue of their dependency on the respective independent claims.

Claims 5 and 39-58 have also been rejected for being "so broad as to encompass any method of producing a xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of gumB and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and G in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation."

Initially, applicants respectfully disagree with the Examiner's characterization (at pages 3-4 of the Office Action) of the invention as the mutant *X. campestris* 2895 lacking wild-type *gum* genes having a plasmid comprising *gumB* and *gumC* genes, but not genes encoding *orfX* or *gumD, E, F* and *G*." The specification at page 7, [29], explains that the aforementioned mutant was used to make the genomic library of the wild type *X. campestris*, NRRL B-1459 from *E. coli* S17-1 to said mutant. Further on the same page, it states that one of the cosmids contains a 16-kb fragment comprising the complete *gum* region. From this fragment, a 4026 bp fragment was cloned for construction of the final plasmid pBBR5-BC, as set forth on page 9, [30] of the originally filed specification. Expression of GumB and GumC protein from the final plasmid were confirmed by introducing said plasmid into *X. campestris* mutant 1231, in which the entire gum gene was deleted. *See* specification at p. 9, [33]. Table 2 at page 10 of the specification lists the strains of *X. campestris* which were used in the study described in the specification. Further, the specification at page 11, [38], describes the *X. campestris* strain XWCM1/pBBR5BC

– the final plasmid containing the gum promoter and *gumB* and *gumC* genes (See specification, p. 9, [31]) – as the strain with multiple, plasmid encoded copies of the *gumB* and *gumC* genes. (emphasis added). Whereas, the *X. campestris* strain XWCM1 was the mutant strain without multiple, plasmid encoded copies of the *gumB* and *gumC* genes. Id., at p. 11. [38]. (emphasis added).

As discussed in the specification, the amount of gene product of *orfX* is not selectively increased in the *X. campestris* strain. See specification, p. 3., [12]. Likewise, the amount of a product of a gene selected from the group consisting *of gumD-gumG, i.e., gumD, gumE, gum F* and *gum G*, is not selectively increased. *See Id.* These descriptions indicate that these respective genes are present in the *X. campestris* strain and said genes encode the respective gene products, *i.e.,* OrfX, GumD, GumE, GumF and GumG.

It is believed that the scope of the amended claims is commensurate with the enablement provided by the originally filed specification. Reconsideration and withdrawal of this rejection is requested.

Written Description

Claims 5 and 39-58 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement due to claim(s) containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleges that "Claims 5 and 39-58, as interpreted, are directed to a genus polypeptides of *gumB* and *gumC, i.e.*, a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, F* and G in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation. The Examiner asserts that "in the instant case, there is no structure correlated to associated function recited in claims with regard to a methods, of producing xanthan using the members of the genus

polypeptides of *gumB* and *gumC* having no structural limitations." The Examiner also asserts that "due to the fact that the specification only discloses the structure of an enzymatically active the structure of an enzymatically active wild-type gene product of *gumB* and *gumC* (wildtype gene accession # *gumB: XCC2454* and wild-type *gumC* gene accession # *XCC2453,* page 8, Table I of specification) in a method for producing xanthan, and the lack of description of any additional species/variants/mutants from any source by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention."

As discussed above, the independent claims have been amended to recite the selective increase in specified gene products encoded by *gumB* and *gum C.* Therefore, the amended claims recite "specific structures" of the respective gene products.

Also discussed above, the *X. campestris* strain, comprises the gene *orfX*, which is not selectively increased in the *X. campestris* strain, as well as the genes encoding the respective gene products, *i.e.,* GumD, GumE, GumF and GumG, whose respective amounts of gene product are not selectively increased. See specification, p. 3., [12.

Applicants note that Table 1 of the specification at page 10, lists xanthan export as the putative function of *gumB* and *gumC* gene products, but no enzymatic activity is described specifically. *See also* Becker et al., Appl. Micrbiol. Biotecnol. (1998) 50:145-152, at 148 (describing gene products of *gumB* and *gumC*, as well as *gumE*, as the products [that] "may be needed for polymerization or export of the polymer.")

For the reasons discussed above, applicants respectfully request withdrawal of the aforementioned rejections under 35 U.S.C. 112, first paragraph.

Rejection under 35 U.S.C. § 103(a)

Claims 5, 39-42 and 48-58

Claims 5, 39-42 and 48-58 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Hassler et al., (1990) and in view of Becker et al., (1998). The Examiner

asserts that Hassler et al., teach a set of mutants of *Xanthomonas campestris* defective in the xanthan biosynthetic pathway, which are capable of producing variant xanthans, which have rheological properties that are different from wild-type xanthan and that one could achieve altered forms of xanthans in specifically tailored mutants of *Xanthomonas campestris,* wherein alterations in the acetylation or pyruvylation or elimination of certain sugar residues in xanthans have major effects on the molecular length, viscosity and polymerization and teach production and purification of xanthans. The Examiner acknowledges that Hassler et al., is silent on the details of specific genes of the pathway that could be altered to achieve the production of xanthan with desired properties. The Examiner states that Becker et al., have laid out the biochemical assignments for all the genes involved in the xanthan biosynthetic pathway in *Xanthomonas campestris,* i.e., the sequential reactions that take place in an orderly manner to synthesize xanthan and the gene order in the xanthan operon/genetic loci (citing Entire document, especially Fig. 2, page 147; Fig. 3, page 148), and that specifically the reference teaches that gene products *of gumB* and *gumC* are involved in the terminal stages of xanthan biosynthesis and regulate the xanthan export and polymerization of the molecule. According to the Examiner, this reference also suggests that elimination of unwanted by-products by genetic modifications of production strains may simplify the recovery of xanthan from the fermentation liquid (citing Perspectives section, page 150).

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et al., and Becker et al., to produce a xanthan of desired molecular length and viscosity by selectively increasing the amount of gene product of *gumB* and *gumC* by introducing additional copies of *gumB* and *gumC* genes into xanthan producing *Xanthomonas campestris.* The Examiner further alleges that motivation to do so derives from the fact that improved and cost effective methods for synthesis of xanthan molecules having certain molecular length and increased viscosity to be used as an additive in the production of number of beneficial compounds in food and pharmaceutical industry. The Examiner alleges that the expectation of success is high, because Hassler et al., and Becker et al., teach the effective use of genetic engineering approaches and the role of specific genes/gene loci in the xanthan biosynthetic pathway.

Applicants respectfully traverse the Examiner's rejection. Initially, applicants note that Hassler's mutants are defective in the xanthan biosynthetic pathway, and Hassler specifically shows that acetylation and pyruvylation can affect the viscometric properties of xanthan. The claimed invention relates to over-expression of two specific *gum* genes, namely *gumB* and *gumC*, which over-expression is unrelated to the mutation of the biosynthetic pathway of xanthan production, nor to any defects in the synthesis of xanthan polymer. Becker et al. provides a discussion of the proposed biosynthetic pathway for xanthan, with hypothesized roles for *gumB* and *gumC* gene products in polymerization or export of the polymer. The Examiner has not explained how the mutations of Hassler et al. when combined with Becker's discussion of a potential biosynthetic pathway would lead one of skill to arrive at the over-expression (increasing the amount of gene product) of any specific gene products, let alone of the particularly claimed *gumB* and *gumC* gene products. The Examiner has not provided a nexus between the mutations provided by Hassler and Becker's proposed biosynthetic pathway to arrive at the subject matter of the pending claims. Moreover, Hassler et al. and Becker et al , when combined, do not teach or suggest: (1) any over-expression of a specific gene or genes of *X. campestris*, or (2) that over-expression of both *gumB* and *gumC* would result in increased viscosity of the produced xanthan product, as claimed. The combination of the cited references also does not teach or suggest any range of molecular lengths of xanthan molecules, *e.g.,* wherein at least 5% of the xanthan molecule population has a length of at least 3 um as measured by atomic force microscopy, as recited in claim 5. For these reasons, one of skill in the pertinent art of xanthan polymer preparation would have no expectation of success of arriving at the subject matter claimed by combining Hassler et al. and Becker et al.. Accordingly, the combination of these cited publications does not render claims 5, 39-42 and 48-58 obvious under 35 U.S.C. 103.

Claims 43-46

Claims 43-46 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over the combination of Hassler et a!., (1990) and Becker et al., (1998) and further in view of Katzen et al., (1998). According to the Examiner, the combination of Hassler et al., (1990) and Becker et al., (1998) does not specifically teach an extrachromosomal element in the form of a plasmid comprising the *gumB* and *gumC* genes that can be used to generate stable integrants in a host cell *i.e., Xanthomonas campestris.* But, the Examiner states, the use of plasmids to alter

gene expression was well known in the art. (citing Katzen et al. as allegedly teaching methods for generation of *Xanthomonas campestris* mutants and the effects of a combination of certain *gum* and non-gum gene mutations, using plasmids (episomal/extrachromosomal or plasmids capable of integrating into genome of the host) comprising one or more copies of desired xanthan biosynthetic pathway genes (citing Results section, column 2, page 1608; and entire document). The Examiner asserts that it would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et aL, (1990) and Becker et al., (1998) and Katzen et al., (1998) to use plasmids comprising one or more copies of *gumB* and *gumC*, for which motivation allegedly derives from the fact, that plasmids are an easy way to increase protein expression. Moreover the Examiner asserts that the expectation of success is high, because the use of plasmids for protein expression was well known, as taught by Katzen et al.

Applicants respectfully traverse the Examiner's rejection and maintain that claims 43-46 are not obvious over the above-cited combination of three publications. The discussion of Hassler et al. and Becker et al., above, is hereby incorporated. Katzen et al. describes potential lethality to cell from elevated amounts of lipid-linked intermediates, which accumulate in the absence or deficiency of one of *gumB*, *gumC* and *gumE*. *See* p. 1615, Col. 2, first paragraph. But nowhere does Katzen suggest that over-expression of both gumB and gumC would be advantageous in the preparation of xanthan polymer, *e.g.,* to increase viscosity of xanthan produced with such over-expression. None of the cited publications suggest the use of extrachromosomal plasmids to over-express *gumB* and *gumC*, thus, the asserted general knowledge "that plasmids are an easy way to increase protein expression," would not direct one of skill to select the genes *gumB* and *gumC*, as the specific genes whose gene product should be over-expressed to obtain a desirable xanthan polymer with increased viscosity, as claimed. One of skill in the art, thus, would not expect the addition of Katzen to the above-cited combination of Hassler and Becker to produce the enhanced xanthan, which is produced as a result of cells over-expressing both of these gene products. Therefore, Katzen does not cure the deficiencies of the combination of Hassler and Becker, as discussed above, and , does not render claims 43-46 obvious in light of the combination of these three cited publications.

Claim 47

Claim 47 has been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over the combination of Hassler et al., (1990), Becker et al., (1998), Katzen et al., (1998) and further in view of Feinbaum R (1998). The Examiner acknowledges that the combination of Hassler et al., (1990), Becker et al., (1998) and Katzen et al., (1998) does not specifically teach a plasmid comprising the *gumB* and *gumC* genes under the control of an inducible promoter. The Examiner asserts that Feinbaum teaches the structure and method of incorporation of inducible promoters into various plasmid constructs and the regulation of gene of interest expression via the inducible promoters through chemical and physical means. The Examiner concludes that it would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et al., (1990), Becker et a!., (1998), Katzen et al., (1998) and Feinbaum R (1998) to use plasmids comprising one or more copies of desired xanthan biosynthetic pathway genes under the control of inducible promoter and that motivation to do so derives from the fact, that an inducible promoter precisely controls the expression of the gene of interest as opposed to a constitutive promoter wherein the gene of interest is constantly in the "on" mode, which in certain cases could be toxic to the host cell. In addition, the Examiner states that an inducible promoter gives a handle to control the expression of gene of interest depending on experimental needs: for example, during specific cell-cycle phase or following the addition of certain factors/supplements that can be converted by the polypeptides of expressed genes to yield products with defined characteristics. The Examiner alleges that the expectation of success is high, because Feinbaum teaches the structure of inducible promoters, the method of incorporation of inducible promoters into various plasmid constructs and the regulation of expression of the gene of interest via the inducible promoters through chemical and physical means.

Applicants respectfully traverse the Examiner's rejection. Applicants reiterate the discussion above with respect to the combination of Hassler et al., Becker et al. and Katzen et al. Feinbaum's general description of plasmids, does not, without more, suggest the over-expression of two specific genes, *gumB* and *gumC,* as claimed. Feingold's discussion of structure of inducible promoters and method of their incorporation into various plasmid constructs and the regulation of gene of interest expression via the inducible promoters through chemical and physical means does not suggest to one of skill in the art which particular gene products are to be

over-expressed through the use of a plasmid comprising one or more copies of the *gumB* and *gumC* genes. Feinbaum's general description of plasmid biology, including inducible promoters, does not add to the combination of the three above-discussed publications, to arrive at the claimed subject matter, which specifically achieves the over-expression of *gumB* and *gumC*. Neither does Feinbaum provide a suggestion or teaching that this particular over-expression of the claimed gene products would provide an improved xanthan polymer, *e.g.*, one with increased viscosity relative to the viscosity of xanthan produced by a wild-type strain of *X. campestris*. Since Feinbaum fails to provide such a teaching, it too, does not remedy the deficiencies of the combined disclosures of Hassler et al., Becker et al. and Katzen et al., to arrive at the claimed method of producing xanthan having an increased viscosity relative to that produced by the wild-type strain, wherein the selectively increasing the amount of gene product is performed by inducing *gumB* and *gumC* using an inducible promoter. Accordingly, the addition of Feinbaum to Hassler et al., Becker et al. and Katzen et al. also would not provide one of skill any expectation of success of arriving at the claimed subject matter. Therefore, claim 47 is not obvious over the above-cited combination of three publications in view of Feinbaum.

For the above-discussed reasons, applicants respectfully request withdrawal of the aforementioned rejections under 35 U.S.C. 103.

CONCLUSION

In view of the foregoing, it is believed that the subject application is in condition for allowance, a notice of which is earnestly solicited by applicants.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: August 21, 2007

Scott F. Yarnell
Registration No. 45,245

Phone: (703) 714-7502
Fax: (703) 714-7410

Hunton & Williams LLP
Intellectual Property Department
1900 K Street, N.W.
Suite 1200
Washington, D.C. 20006-1109
Ph. (202) 955-1500
Fax (202) 778-2201